NSHS BETHESDA INSTRUCTION 6000.41B

From: Commanding Officer, Naval School of Health Sciences, Bethesda

Subj: CLINICAL INVESTIGATION PROGRAM (CIP)

Ref: (a) BUMEDINST 6000.12A
(b) 32 CFR Part 219
(c) NAVMEDCOMINST 6320.3B
(d) BUMEDINST 6710.69
(e) DoD Directive 3216.1 Use of Laboratory Animals in DoD Programs
(f) SECNAVINST 3900.39B
(g) OASD(HA) Memo Department of Defense (DoD) Guidance for Assurance of Compliance with the Federal Policy for the Protection of Human Subjects of 10 Jun 93 (NOTAL)

Encl: (1) Navy Clinical Investigation Program Guidebook

1. Purpose. To update implementation of the Clinical Investigation Program (CIP). This instruction contains detailed information about funding, preparation of clinical investigation protocol packages, review and approval processes, Clinical Investigation Department (CID) management reports, annual site visits and audits by the Naval School of Health Sciences (NSHS) Bethesda and formats used in the CIP. This issuance is a substantial revision and should be reviewed in its entirety.

2. Cancellation. NSHSBETHINST 6000.41A

3. Total Quality Leadership Principles. The Navy CIP supports the strategic plan, vision, and mission of the Navy Medical Department and NSHS, Bethesda. The CIP vision includes the following objectives:

a. Improve the quality of health care for Navy, Marine Corps, and all other Department of Defense (DoD) beneficiaries.

b. Generate an atmosphere of scientific inquiry.

c. Promote an academic environment of high professional standing.

d. Support accreditation of Graduate Medical Education programs.

4. Policy. NSHS Bethesda serves as Program Manager for clinical investigations conducted at Navy medical and dental treatment facilities (MTFs and DTFs), as directed by reference (a). The approval and conduct of human subjects research complies with the Federal Policy for the Protection of Human Subjects, as promulgated by reference (b). Additionally, Navy CIP policies are consistent with directives issued by the DoD, Secretary of the Navy (SECNAV), Bureau of Medicine and Surgery (BUMED), and with applicable regulations of other federal agencies (e.g., Food and Drug Administration (FDA) and Health and Human Services (HHS)). The following policies pertain:

a. Navy Department personnel are prohibited from accepting any compensation in addition to their salaries for the conduct of clinical investigations.

b. All clinical investigations are subject to military contingency requirements.

c. If an individual entitled to medical care and enrolled as a human subject loses his or her eligibility for care (e.g., the subject or subject's sponsor separates prior to retirement), and if the subject's continued participation in an investigation is likely to be beneficial to his or her medical well-being (e.g., enrollment in an oncology group protocol):

(1) Apply for Secretary of the Navy designee status for the subject if there is a Navy site in the subject's community where that study is active, or

(2) Attempt to transfer the subject to a nonmilitary facility in their community where that study is active.

d. Activities may not compete with available commercial facilities in providing special services to agencies outside the federal government.

e. Data collected in a CIP study are the property of the Navy Department. Release of this data is not authorized without clearance by the proper approval authority. To be released, data must be for the benefit of medical science and not for the profit of private individuals. All manuscripts must have a statement within the text acknowledging that the interpretative findings and opinions are those of the author(s) and not of the Navy.

f. CIP investigators may not maintain custody of funds or other resources that support the program. Those resources must

remain under the cognizance of the comptroller at the principal investigator's medical or dental treatment facility (MTF or DTF), or by a third party specified in an approved resource sharing agreement.

g. Every CIP project shall include an arrangement for treatment of any project-related injuries. Reference (a) specifies that only persons entitled to care in MTFs are eligible to participate as human subjects. When justified, waiver requests can be considered at BUMED, provided documented alternate arrangements exist for the treatment of project-related injuries. Those arrangements may be either the provision of Secretarial designation as DoD health care beneficiaries, or binding obligations for benefits equivalent to those available to DoD health care beneficiaries. Secretarial designee status may be granted to nonbeneficiary subjects in officially approved clinical research studies subject to the capabilities of the professional staff of the MTF and the availability of space and facilities, per reference (c).

h. CIP investigators who plan collaborations with colleagues at other institutions must provide evidence of approval by the other activity. Institutional Animal Care and Use Committee (IACUC), and/or Committee for the Protection of Human Subjects (CPHS)/Institutional Review Board (IRB) approval should be documented, as applicable. A copy of an appropriately executed Letter of Intent, Memorandum of Understanding, Cooperative Research and Development Agreement or other resource sharing agreement, with local comptroller, Judge Advocate General, and Commander/Commanding Officer (CO) endorsement, is required.

i. Studies that may require submission of Navy prepared investigational new drug applications or new device exemption requests to the FDA will be reviewed and approved in accordance with references (a) and (d). Since Navy investigators are transient and enrolled subjects must be guaranteed follow-up treatment, the CO of the MTF or DTF at the intended site of performance, rather than the principal investigator of the proposed study, must be designated as the sponsor to the FDA.

j. Navy Department personnel may not solicit gifts or contributions intended to benefit the Navy unless authorized by SECNAV. Grant applications must be signed by the CO of the MTF/DTF. Donors and grantors must be notified in writing that their gift/grant must be made to the Government on behalf of the MTF/DTF, and is not for the personal use of any individual.

k. All laboratory animal research performed in DoD component facilities, or sponsored by the DoD or by its components, shall comply with reference (e). The BUMED Special Assistant for

Veterinary Medicine (MED-02E) requires that protocols proposing the use of non-human primates, cats, dogs or marine mammals must be submitted for review to MED-02E after local IACUC review is completed. If approved by MED-02E, the protocol may be implemented when approved by the CO of the local MTF/DTF. Other animal studies do not require prior approval from MED-02E. One copy of each locally approved animal protocol will be sent for information and reference to (1) MED-02E and (2) NSHS Bethesda, Code OC.

l. All retrovirology research (HIV-l, HIV-2, or HTLV-l) requires approval by the BUMED Human Immunodeficiency Virus (HIV) Program Division (MED-02H). To expedite review, study packages may be forwarded to MED-02H and to the CPHS/IRB concurrently. However, if either the CPHS/IRB or MED-02H require changes, written approval of the change must be obtained from the other party before routing to the MTF/DTF CO for final approval.

m. Per reference (a), the CO, NSHS Bethesda may delegate authority annually to the COs of MTFs/DTFs for local approval of all clinical investigations except for those involving dogs, cats, non-human primates, marine mammals, retrovirology research, and investigations requiring Assistant Secretary of the Navy (Research, Development and Acquisition) approval, per reference (f). Delegation of approval authority will be based on satisfactory annual inspection of the local program.

n. All CIP projects receive second level review at NSHS Bethesda for administrative completeness and compliance with relevant higher authority directives and guidance. Apparent discrepancies must be resolved to the satisfaction of the CO, NSHS Bethesda. Approved research must be conducted in accordance with all relevant Navy and federal policies, and be consistent with prevailing ethical guidelines (i.e., Belmont Report, Nuremberg Code, World Medical Association Declaration of Helsinki, etc.). For all research involving human subjects, a medical monitor shall be appointed by name if either the IRB or the approval official determines the risk to be more than minimal. Additional guidance is provided in enclosure (1).

o. All Navy MTFs and DTFs must have an approved Assurance of Compliance with the Federal Policy for the Protection of Human Subjects on file before using human subjects in research. For the Navy CIP, NSHS Bethesda is responsible for approval of Assurance applications and for issuing a DoD Assurance number. References (b) and (g) pertain. Further guidance is provided in enclosure (1).

5. Summary. The opportunity to conduct clinical research has become an integral part of supporting excellence in health care

delivery to patients and providing quality education to the professional staff. Enclosure (1) is an essential reference for all Medical Department personnel involved with implementing, administering and conducting clinical investigations at Naval MTFs and DTFs. It should be widely distributed. The staff at local CIDs and at NSHS Bethesda (Code OC) are available to provide assistance and additional guidance to all CIP participants.

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Distribution:
List I
BUMED WASHINGTON DC (MED 02H)
BUMED WASHINGTON DC (MED 02E)
BUMED WASHINGTON DC (MED 05B)
All MTFs and DTFs